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Abstract

The United States Department of Defense medical planners need survival-time estimates for anticipated patient streams associated with projected combat scenarios. Survival-time estimates should be grounded in empirical observations. Unfortunately, research in this domain has been limited to a single paper describing the development of died-of-wounds curves for combat casualties with life-threatening injuries. The curves developed from that research were based on a small dataset ($n = 160$, with 26 deaths and 134 survivors) of forward surgical (Role II) casualties and subject matter experts' judgments. This paper reports the first empirically based time-to-death curves for combat casualties based on a large sample. The results indicate that survival time varied across roles of care at which casualties died but was at most weakly associated with injury severity. Time-to-death curves were, therefore, developed for the overall study population of valid times to death and for Role I, Role II and Role III care. The log-logistic probability distribution provided the best representation of the survival times for the overall study population, while the log-normal distribution was the best choice for Role I, Role II and Role III care. The proposed time-to-death curves should refine the survival-time estimates used in combat medical logistics planning.

Keywords

Time to death, combat mortality, statistical modeling, log-normal probability distribution

1. Introduction

The United States Department of Defense (DoD) medical planners need logistics tools to plan for projected combat scenarios. These tools must optimize the configuration of the medical treatment facility (MTF) network within combat zones. Optimization depends on appropriate facility locations and availability of staff, equipment, supplies and evacuation assets at each MTF. Successful optimization ensures that combat casualties receive appropriate treatment as quickly and cost-effectively as possible.

The MTF network design has a hierarchical structure with casualties moving from point of injury (POI) to first-responder care (Role I), forward-resuscitative care (Role II), theater hospitalization (Role III) and definitive care (Role IV).¹ Medical care capabilities increase as the casualty moves through the network. Medical resource planning must ensure that facilities have the resources to fulfill their planned functions.

Sound casualty stream projections are essential to effective medical logistical planning. The casualty stream is characterized by the case mix of casualties and its evolution over time. The types of injury requiring treatment determine the case mix. Logistics planning uses simulation tools to estimate case mix and the distribution of those cases over time. Resource requirements estimates are derived by combining those estimates with treatment protocols that specify the types of care and resources needed to treat each injury or illness.

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Definitive survival-time estimates are not currently available for casualty stream projections. Ideally, these estimates should be based on empirical survival evidence. Empirically based estimates accurately reflect events as they occur in combat operations. Unfortunately, research in this domain has been limited. A literature review identified only a single paper,² which presented survival curves for combat trauma casualties with life-threatening injuries. Those curves were based on a small dataset ($n = 160$, with 26 deaths and 134 survivors) of Role II casualties. Subject matter experts (SMEs) imputed missing evacuation times in about 38% of the survivor cases. Nevertheless, the survival curves in the paper reflected the empirical data of early combat operations in Iraq as well as the experiences of military medical doctors.³

This paper reports the development of empirically based time-to-death curves for combat trauma casualties based on a large sample. The curves are based on deaths in Iraq and Afghanistan combat operations between 2002 and 2011. These analyses address three questions concerning the time from injury to death: What is the overall time-to-death curve? Does injury severity affect the curve? Is the curve the same for all treatment roles of care?

2. Methods

This study was conducted in compliance with all applicable federal regulations governing the protection of human subjects in research and was approved by the Institutional Review Board at the Naval Health Research Center (NHRC), San Diego (Protocol No. NHRC.2003.0025).

2.1. Data source

A total of 4491 electronic casualty death records are stored in the Expeditionary Medical Encounter Database (EMED), formerly known as the Navy-Marine Corps Combat Trauma Registry,⁴ at the NHRC. These records cover Iraq and Afghanistan combat operations between March 2002 and March 2011.

Figure 1 depicts the selection criteria for casualties in this study. Casualties with times to death of zero ($n = 1183$) were excluded from this study. Casualties were excluded if time to death could not be determined from the record (missing, $n = 225$). Casualties were excluded when the recorded times produced a negative time to death ($n = 128$). Casualties were excluded if they died more than 72 hours after injury ($n = 104$). Those exceptionally long times might be influential data points that would distort the functional form for the large majority of casualty deaths. With these exclusions, the final study population consisted of 2851 casualties for whom valid time-to-death estimates could be computed.

2.2. Time to pronounced death

The record for each fatality indicated the time of injury and the time of pronounced death. The time to pronounced death was computed as the difference, in minutes, between the time of injury and time of pronounced death. It would be expected that the actual time of death in Roles II and III would be the same as the pronounced time of death but not in Role I, where a medical doctor was not generally present and the death would only be pronounced after evacuation to the next role of care was completed.

2.3. Injury severity

The electronic records described all of the injuries suffered by each casualty. The severity of injuries was described using the Abbreviated Injury Scale (AIS),⁵ originally developed to score blunt injuries from automobile accidents.⁶ Over time, the AIS system has evolved to code blunt and penetrating injuries in both civilian and combat trauma. The current AIS version (AIS 2005 Update 2008)⁷ contains over 2000 codes. Each code consists of six digits that indicate the anatomic site and nature of the injury and a seventh digit that indicates injury severity. Severity scores range from "1" for minor injury to "6" for an untreatable injury that generally will result in death.

In this study, injury severity classification was based on the most severe injury. This simple method was adopted to deal with the fact that over 97.5% of combat death casualties suffered multiple injuries. The severity score for the most severe injury is the maximum AIS score (MaxAIS). MaxAIS has been shown to be strongly correlated with mortality⁸ and predicts fatality nearly as well as more complex systems that combine the effects of multiple injuries.^{9–15}

2.4. Role of care

MTFs provide four roles of care based on the medical resources available at a facility. First-responder care (Role I) consists of immediate medical care, resuscitation and stabilization. Role I trauma casualties requiring more extensive treatment are evacuated to a higher role of care, usually within minutes. Forward-resuscitative care (Role II) provides a higher capability for the triage, stabilization and treatment of shock. A typical Role II facility also provides damage-control surgery and recovery facilities for casualties before they are returned to duty (RTD) or evacuated. In-theater hospitalization care (Role III) is a full-fledged field hospital or hospital ship. Role III facilities provide all surgical specialties, advanced emergency, intensive care unit and ancillary services. Role III is the highest level of care in theater. Finally, definitive care is received at Role IV facilities after evacuation from the

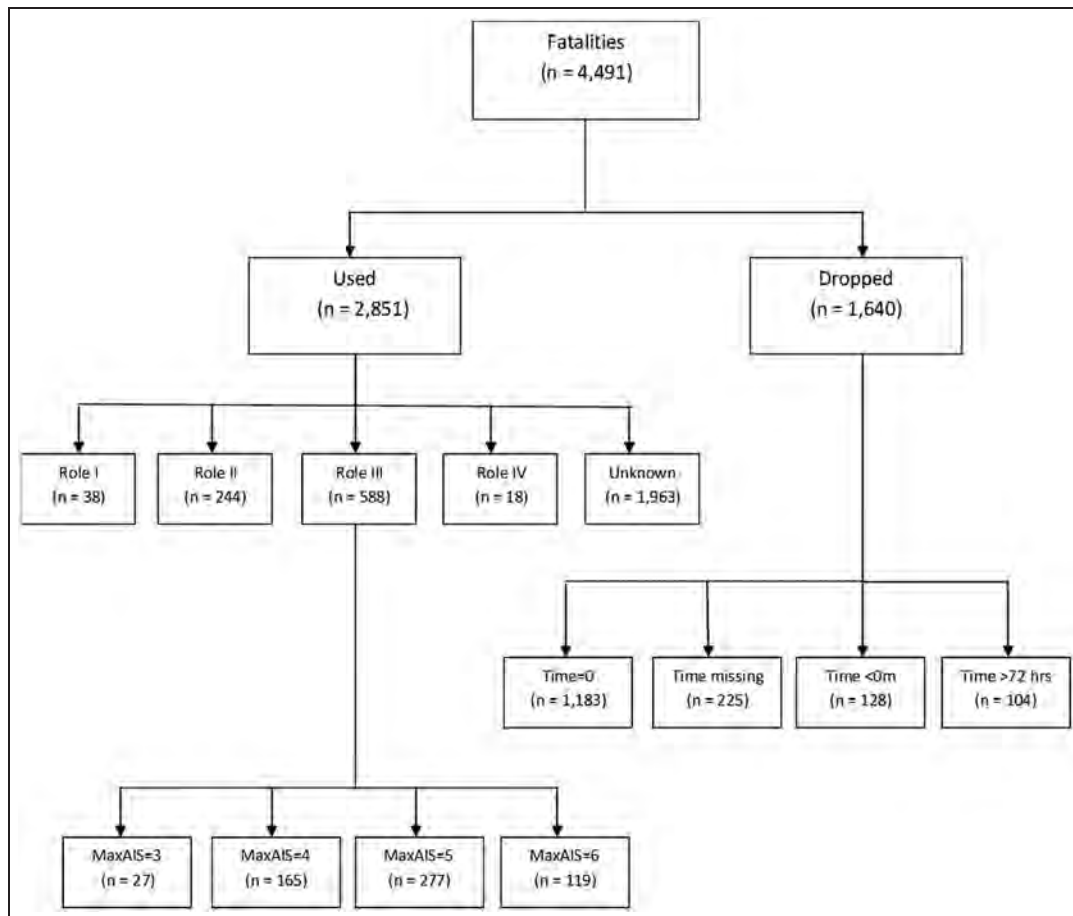


Figure 1. Flow diagram documenting selection criteria used for identifying study population for analysis.

combat theater of operations. Role IV provides a full spectrum of preventative, curative and rehabilitative medical services.

It should be noted that not all patients proceed linearly through the roles of care. They may in fact present for first care at any role of care and frequently do as a function of mode of evacuation, the proximity of the POI to a given MTF, and other factors.

For this study, the role of care at which a casualty died was determined by matching the casualty's death date and time with the appropriate record in the Theater Medical Data Store (TMDS) repository. The TMDS is the most comprehensive registry of patient treatment and flow through the MTF network. This study analyzed fatalities in four groups: (a) all casualties with valid times to death ($n = 2851$); (b) casualties who died at Role I care ($n = 38$); (c) casualties who died at Role II care ($n = 244$); and (d) casualties who died at Role III care ($n = 588$). The role-level analyses could be performed for only 30.5% of the study population fatalities (19.4% of total fatalities) because role of care at time of death could not be determined for the

study population's other fatalities (see Figure 1). The 1963 fatalities (69%) that could not be assigned a role of care were primarily casualties killed on the battlefield that did not receive any medical care.¹⁶

2.5. Statistical analysis

The statistical analyses addressed three questions: (a) What is the overall time-to-death curve? (b) Does injury severity affect the curve? (c) Is the curve the same for all treatment echelons or roles of care?

2.5.1. Survival-time analyses. Survival-time analyses tested for survival-time differences as a function of injury severity and as a function of role of care. Kaplan-Meier (K-M) estimators provided the hypothesis tests. Survival probability was plotted against time to death. A log-rank statistical test assessed differences among the time-to-death curves for different groups. Separate tests assessed survival-time differences as a function of injury severity and role of care.

The tests included pair-wise comparisons between groups. Tukey's method¹⁷ adjusted significance tests to allow for multiple comparisons.

2.5.2. Survival-time modeling. Using survival-time modeling, mathematical functions were developed to approximate the observed survival-time distributions. The available literature¹⁸ suggested that time to death is a monotonically declining survival function. However, the available information is too limited to confidently state the form of that function. Consequently, five candidate *Accelerated Failure Time* models¹⁸—exponential, weibull, log-normal, log-logistic and generalized gamma—were fitted to the data using maximum likelihood procedures. Each model was a variant of Equation (1):

$$\log T_i = \beta_0 + \sigma \epsilon_i \quad (1)$$

T_i is a random variable denoting the time to pronounced death, β_0 is the intercept, ϵ_i is a random disturbance term and σ is a “scale” parameter that describes the shape of the modeled hazard function. The mean and variance of ϵ_i is constant from some distribution and σ represents changes in the disturbance variance. Observations are assumed to be independent of each other. Model choice determines the functional form of the model. For example, the distribution of ϵ_i is normal for the log-normal model, logistic for the log-logistic model and log-gamma for the generalized gamma model. Exponential distributions have a standard extreme-value distribution for ϵ_i with $\sigma = 1$. Like the exponential distribution, the weibull distribution has an extreme-value distribution for ϵ_i but the scale parameter σ is not 1 but greater than zero.

The optimal time-to-death curve function was identified using two criteria: (a) how well the modeled cumulative hazard approximated the empirical K-M cumulative hazard function,¹⁹ and (b) the Akaike information criterion (AIC).²⁰ Criterion (a) was based on the residual sum of squares (RSS) of the modeled cumulative hazard and the empirical K-M cumulative hazard, and a visual inspection of the time plot of the difference of the cumulative hazards. When the criteria supported different models, criterion (a) determined the final model selection.

Data management and statistical analyses were carried out using SAS software, Version 9.3 (SAS Institute, Cary, North Carolina).

3. Results

3.1. Injury severity

All of the casualties suffered at least one serious injury (MaxAIS ≥ 3). However, most of the casualties suffered more severe injuries. Injury severity distributions were broadly comparable for the full sample and the

Table 1. Maximum injury severity (MaxAIS) distribution.

Characteristic	No. (%)
Total sample	
3 – Serious	89 (3.1)
4 – Severe	644 (22.6)
5 – Critical	1246 (43.7)
6 – Untreatable	869 (30.5)
Missing	3 (0.1)
Role I	
3 – Serious	3 (7.9)
4 – Severe	7 (18.4)
5 – Critical	18 (47.4)
6 – Untreatable	10 (26.3)
Role II	
3 – Serious	6 (2.5)
4 – Severe	77 (31.6)
5 – Critical	114 (46.7)
6 – Untreatable	47 (19.3)
Role III	
3 – Serious	27 (4.6)
4 – Severe	165 (28.1)
5 – Critical	277 (47.1)
6 – Untreatable	119 (20.2)
Role uncertain	
3 – Serious	52 (2.6)
4 – Severe	391 (19.9)
5 – Critical	826 (42.1)
6 – Untreatable	691 (35.2)
Missing	3 (0.2)

Note: Injury severity distributions for the total casualty sample ($n = 2851$) and for Role I ($n = 38$), Role II ($n = 244$), Role III ($n = 588$), and Role uncertain ($n = 1963$) casualty subsets.

role-specific casualty subsets (Table 1). However, the severity distributions for Roles I, II and III differed from the distribution for cases whose role of care at time of death could not be determined from the records. A two-way classification of cases by severity and role demonstrated that the differences among the four groups were small, but statistically significant ($\chi^2 = 78.17$, 9 *df*, $p < .001$).

The group differences were significant only when comparing unknown role cases and the known role cases. The Role I, II and III differences were trivial and not statistically significant ($\chi^2 = 6.25$, 6 *df*, $p = .396$).

A higher proportion of MaxAIS = 6 injuries was the primary difference between the unknown role cases and the known role cases. The severity distribution for the unknown role of care included 90 more MaxAIS = 6 cases than expected ($\chi^2 = 13.26$, 1 *df*, $p < .001$). This difference contrasted with fewer than expected cases for MaxAIS = 3 (9 cases, $\chi^2 = 1.26$, 1 *df*, $p = .262$), MaxAIS = 4 (52 cases, $\chi^2 = 6.11$, 1 *df*, $p = .013$) and MaxAIS = 5 (28 cases, $\chi^2 = 0.93$, 1 *df*, $p = .335$).

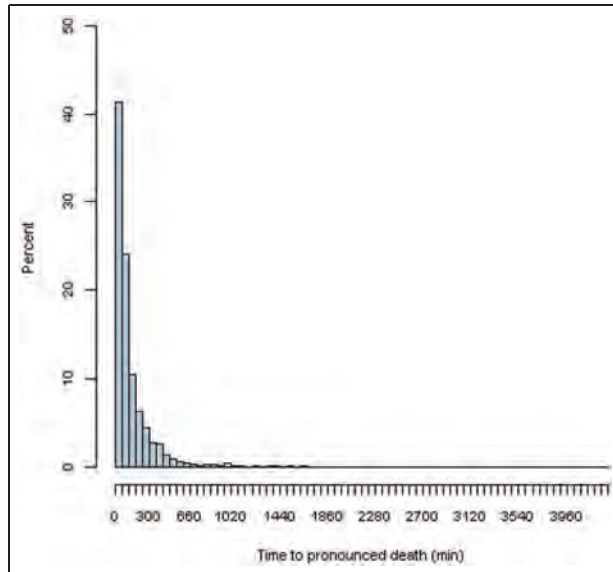
The known role severity distributions reversed the unknown role severity profile. Those distributions had fewer than expected MaxAIS = 6 cases and more than

Table 2. Statistics of times to death (in minutes).

Role of care	N (%)	Mean	Median	Std dev	Min	Max	IQR	95th percentile
Role I	38 (1.3)	130.2	60.5	142.7	11	495	217	495
Role II	244 (8.6)	94.6	64.0	93.2	2	753	68	278
Role III	588 (20.6)	158.1	73.0	267.9	1	2296	101	575
Unknown	1963 (68.9)	181.1	80.0	365.5	1	4312	155	585
Total	2851 (100.0)	185.1	76.0	401.0	1	4312	136	628

Note. 18 (0.6%) Role IV cases were excluded from analysis.

IQR: interquartile range.

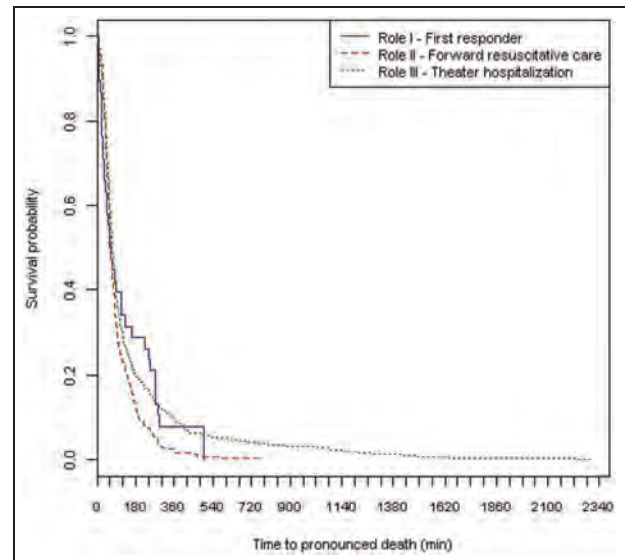
**Figure 2.** Histogram of valid times to pronounced death for the entire study population ($n = 2851$).

expected MaxAIS = 3, MaxAIS = 4 and MaxAIS = 5 cases. On the whole, the differences reflect a lower than expected frequency of MaxAIS = 6 cases in the populations representing known roles of care.

3.2. Time to pronounced death

Figure 2 displays a histogram of the pronounced death times for the 2851 casualty deaths. Approximately 65% of casualties died within 2 hours from the POI and about 82% of casualties died within 4 hours from the POI. Ninety-five percent of all casualty deaths occurred within about 10 hours, with a median time to death of about 75 minutes.

Detailed examination of the time-to-death data indicated two points of interest (Table 2). Firstly, the distributions were severely skewed. The skew evident in Figure 2 applied to the data from all three roles of care. The role-specific skew is evident in median times that are less than the mean and in standard deviations that equal or exceed

**Figure 3.** Comparison of Role I, Role II and Role III Kaplan-Meier time-to-death curves ($n = 870$).

the mean. The differences between roles of care provided the second point of interest regarding the time-to-death distributions. The median survival time increased from Role I to Role III (Table 2). The differences were modest, but statistically significant as evidenced in the “Role” section of Table 3.

3.3. Hypotheses tests

The results of the three hypotheses tests conducted are shown in Table 3 and the associated time-to-death K-M curves are displayed in Figures 3 and 4. For the first hypothesis test, we rejected the null hypothesis that survival time was independent of the role of care at which patients died ($P = 0.001$). The Role I time-to-death curve in Figure 3 is erratic and overall higher than the Role II curve, which is counterintuitive, while the Role II and Role III curves behave as expected. This may be due to the small casualty death counts at Role I and the fact that not all casualties proceed linearly through the roles of care

Table 3. Impact of role and injury severity on survival time.

Hypothesis	Statistical test	χ^2	p-value
1. Role	Log-rank	13.3	0.001*
	I vs. II	9.9	0.005*
	I vs. III	7.5	0.017*
	II vs. III	13.3	0.001*
2. Injury severity	Log-rank	8.9	0.03*
	3 vs. 4	2.7	0.35
	3 vs. 5	2.9	0.33
	3 vs. 6	1.4	0.65
	4 vs. 5	0.0	1.00
	4 vs. 6	0.1	0.99
	5 vs. 6	0.2	0.98
3. Severity \times role			
a. Role II	Log-rank	5.2	0.16
	3 vs. 4	2.3	0.42
	3 vs. 5	3.1	0.29
	3 vs. 6	1.0	0.75
	4 vs. 5	4.1	0.18
	4 vs. 6	3.1	0.29
	5 vs. 6	0.6	0.87
b. Role III	Log-rank	6.6	0.09
	3 vs. 4	1.3	0.67
	3 vs. 5	0.0	1.00
	3 vs. 6	6.0	0.07
	4 vs. 5	0.4	0.91
	4 vs. 6	0.7	0.84
	5 vs. 6	2.2	0.45

*Indicates statistically significant difference using experiment-wise Type I error (alpha) of 5%.

such that higher levels of care may well be seeing a skewed injury sample.

For the second hypothesis test, injury severity was weakly associated with survival time ($P = 0.03$), but pair-wise comparisons showed no significant associations. As shown in the total study population plot in Figure 4, only the MaxAIS 3 curve ($n = 89$ [3%]) was visually distinct from the other curves. The curves for MaxAIS 4, MaxAIS 5 and MaxAIS 6 were so similar that the time required to reach 50% probability of survival was almost identical (75 minutes) for each of them, and the time required to reach 30% probability of survival never differed by more than 22 minutes. Ignoring 4% of data at the extreme end of the tails, the maximum difference was 63 minutes for the MaxAIS 4 and MaxAIS 6 curves at 12% survival probability.

Finally, for the third hypothesis test, we failed to reject the hypothesis of independence between survival time and injury severity within in-theater roles of care ($P = 0.16$ for Role II and $P = 0.09$ for Role III). There were no significant associations between the survival time and injury severity for any of the six pair-wise comparisons at Role II and Role III care. Role I was not considered for this hypothesis test because of low counts ($n = 38$). The Role

II and Role III plots in Figure 4 show the K-M time-to-death curves by injury severity for Role II and Role III, respectively. Interestingly, for Role II we see that all the MaxAIS 3 patients ($n = 6$) die faster than the rest with all the MaxAIS 3 deaths occurring within 300 minutes.

3.4 Survival-time functions

Four sets of survival-time distribution models were examined. One set was based on the entire sample of valid times to death ($n = 2851$). The other three sets were based on deaths that occurred at Role I, Role II and Role III care. Injury severity was ignored because survival time was not significantly associated with severity.

Tables 4 and 5 provide two sets of model-fit statistics for the five candidate survival-probability distributions: (a) RSS for the modeled and empirical K-M cumulative hazard functions (Table 4); and (b) AIC (Table 5). To exclude influential outlier data points, the RSS statistics were computed based on the times to death within the 95th percentile limit for all groups except Role I care, which was based on times within 4 hours from the POI. The log-logistic model provided the best summary of the time-to-death distribution for the entire sample (regardless of role of care) based on RSS, the time plot of the difference in cumulative hazards (Figure 5) and the AIC statistic. The log-normal model was the best choice for role-specific models. In choosing the log-normal model for Role I, Role II and Role III care, the RSS statistic and the associated time plot of the difference in modeled and empirical K-M cumulative hazards (Figure 5) were weighted more heavily than the AIC statistic.

The chosen survival functions (Table 6) closely approximated the actual time-to-death distributions. The total study population plot in Figure 6 illustrates this point by comparing the empirical K-M survival function with the log-logistic function for time to death (t) for all casualty deaths in the study regardless of role of care. The Role I, II and III plots in Figure 6 provide similar comparisons for the log-normal curves for Roles I, II and III, respectively. The location of the actual times to death relative to the function is the critical point in these comparisons. All of the curves demonstrate accurate predictions of observed times to death. The K-M survival function illustrates that this accuracy is achieved despite gaps in the dataset. Those gaps, each of which is indicated by a plateau in the K-M function, identify time periods during which no deaths were observed in this study.

The role-specific curves that would be used in logistics simulations are plots of the general log-normal function:

$$S(t) = 1 - \Phi\left(\frac{\log(t) - b_0}{b_1}\right) \quad (2)$$

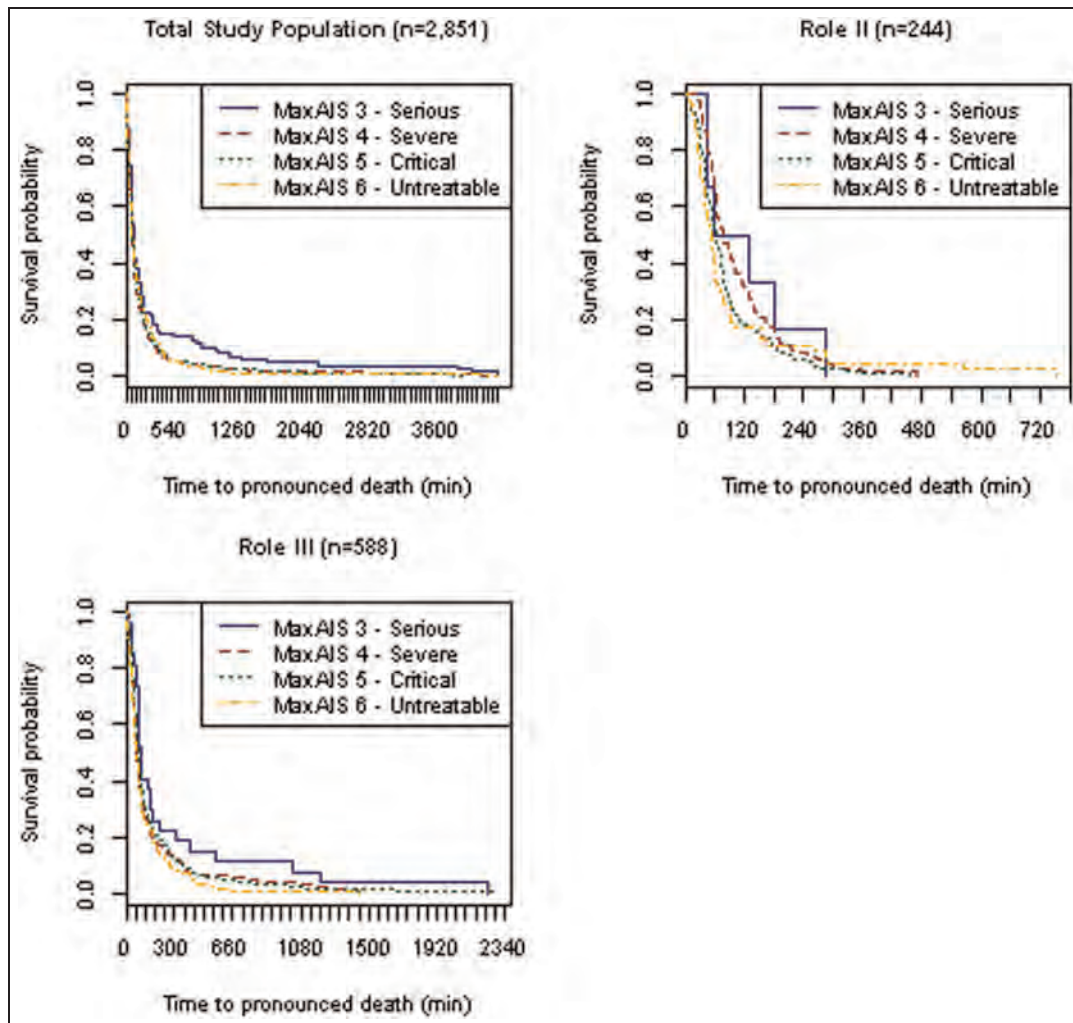


Figure 4. Comparison of time-to-death curves by injury severity (MaxAIS) for entire study population ($n = 2851$), Role II ($n = 244$) and Role III ($n = 588$).

Table 4. Alternative models for survival-time functions based on residual sum of squares (RSS) of modeled and empirical Kaplan–Meier cumulative hazard functions.

Level of care	Residual sum of squares (RSS ^a)				
	Exponential	Weibull	Log-normal	Log-logistic	Gamma
Role I	0.790	0.522	0.398	0.398	NA ^b
Role II	3.232	4.010	0.797	1.243	1.231
Role III	20.646	12.723	3.043	4.281	3.093
All roles	44.654	23.264	4.968	0.934	4.053

^aThe smaller the RSS, the better the model fit.

^bNot computed due to lack of convergence of maximum likelihood estimates.

The ϕ term is the cumulative distribution function for the standard normal distribution. The equation treats the log-transformed survival times as normally distributed with an average of b_0 and a standard deviation of b_1 . The

functions start at one and decline toward zero over time. The b_0 intercept parameter determines the mean survival time. The b_1 scale parameter determines the rate of decline. The function drops more rapidly for smaller b_1

Table 5. Alternative models for survival-time functions based on Akaike information criterion (AIC).

Level of care	Akaike information criterion (AIC ^a)				
	Exponential	Weibull	Log-normal	Log-logistic	Gamma
Role I	126.4	127.9	124.9	128.4	NA ^b
Role II	656.3	642.8	606.8	598.1	607.5
Role III	1977.5	1941.5	1809.9	1772.9	1811.9
All roles	10,641.0	10,078.4	9601.1	9502.4	9592.8

^aThe smaller the AIC statistic, the better the model fit.

^bNot computed due to lack of convergence of maximum likelihood estimates.

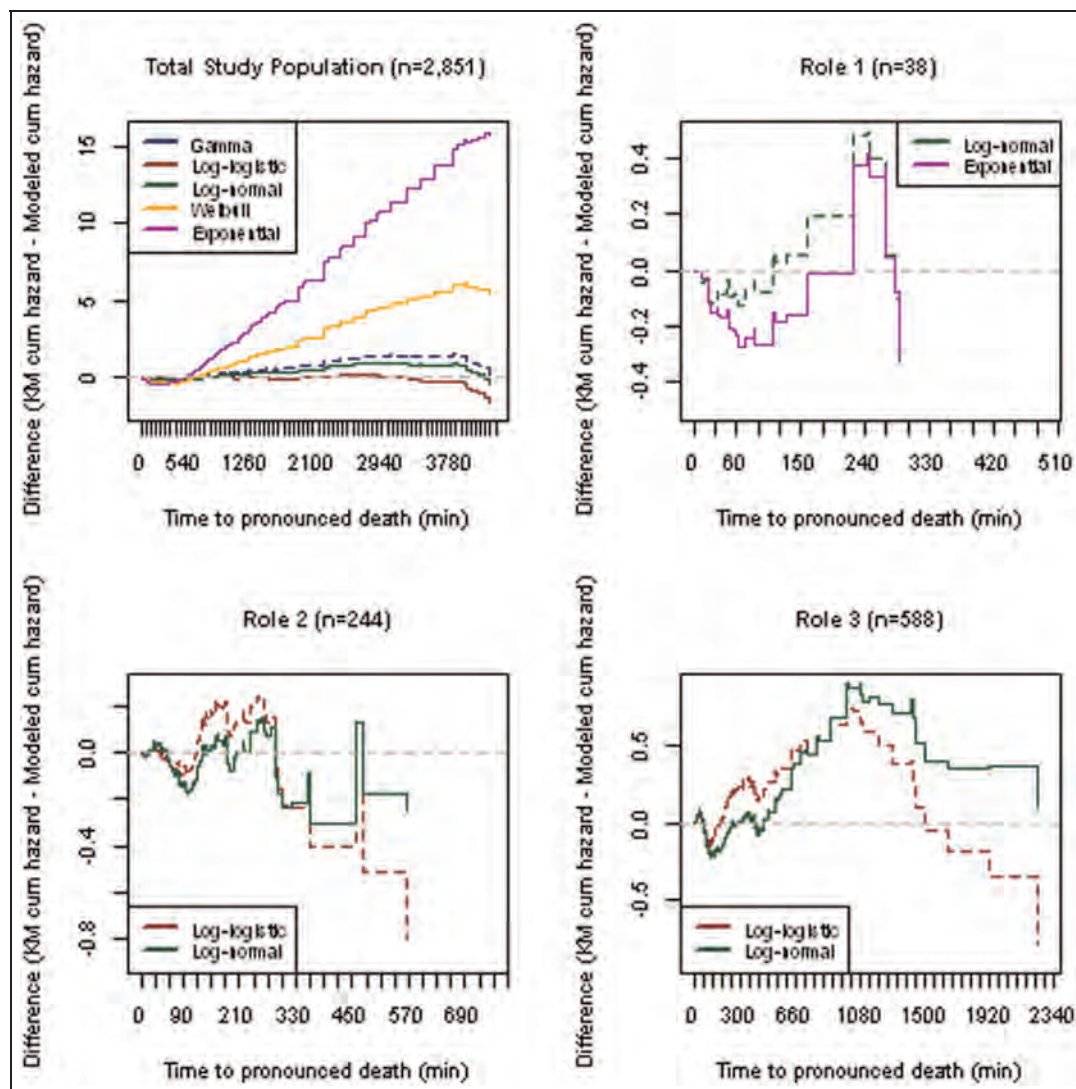


Figure 5. Comparison of the difference between the Kaplan–Meier empirical cumulative hazard and the modeled cumulative hazard for the entire study population ($n = 2851$), Role I ($n = 38$), Role II ($n = 244$) and Role III ($n = 588$).

values. Thus, rate of decline is greatest for Role II ($b_1 = 0.832$), followed by Role III ($b_1 = 1.124$) and Role I ($b_1 = 1.187$), as shown in Table 6. The Role I rate of decline for

the survival function would be expected to be steeper than that of Role II and the unusual behavior of the curve may be attributed to the low casualty counts for Role I ($n = 38$).

Table 6. Parameters of the best-fitting functions.

	Estimate	Standard error	95% Confidence limits	
Full sample^a				
b_0	4.368	0.023	4.323	4.413
b_1	0.713	0.011	0.691	0.735
Role I^b				
b_0	4.233	0.193	3.855	4.610
b_1	1.187	0.136	0.948	1.486
Role II^b				
b_0	4.208	0.053	4.104	4.313
b_1	0.832	0.038	0.762	0.909
Role III^b				
b_0	4.383	0.046	4.292	4.474
b_1	1.124	0.033	1.061	1.190

^aLog-logistic model.^bLog-normal model.

For simulations of casualty deaths in the overall population regardless of the role of care, the log-logistic survival function in Equation (3) can be employed:

$$S(t) = \frac{1}{1 + \alpha t^\gamma} \quad (3)$$

where $\alpha = e^{(-b_0/b_1)}$ and $\gamma = 1/b_1$

The b_0 intercept parameter determines the mean of the log-transformed survival times while the b_1 scale parameter determines the rate of decline of the survival function. The function drops rapidly for smaller b_1 values. Parameter values for the function are $b_0 = 4.368$ and $b_1 = 0.713$ (Table 6).

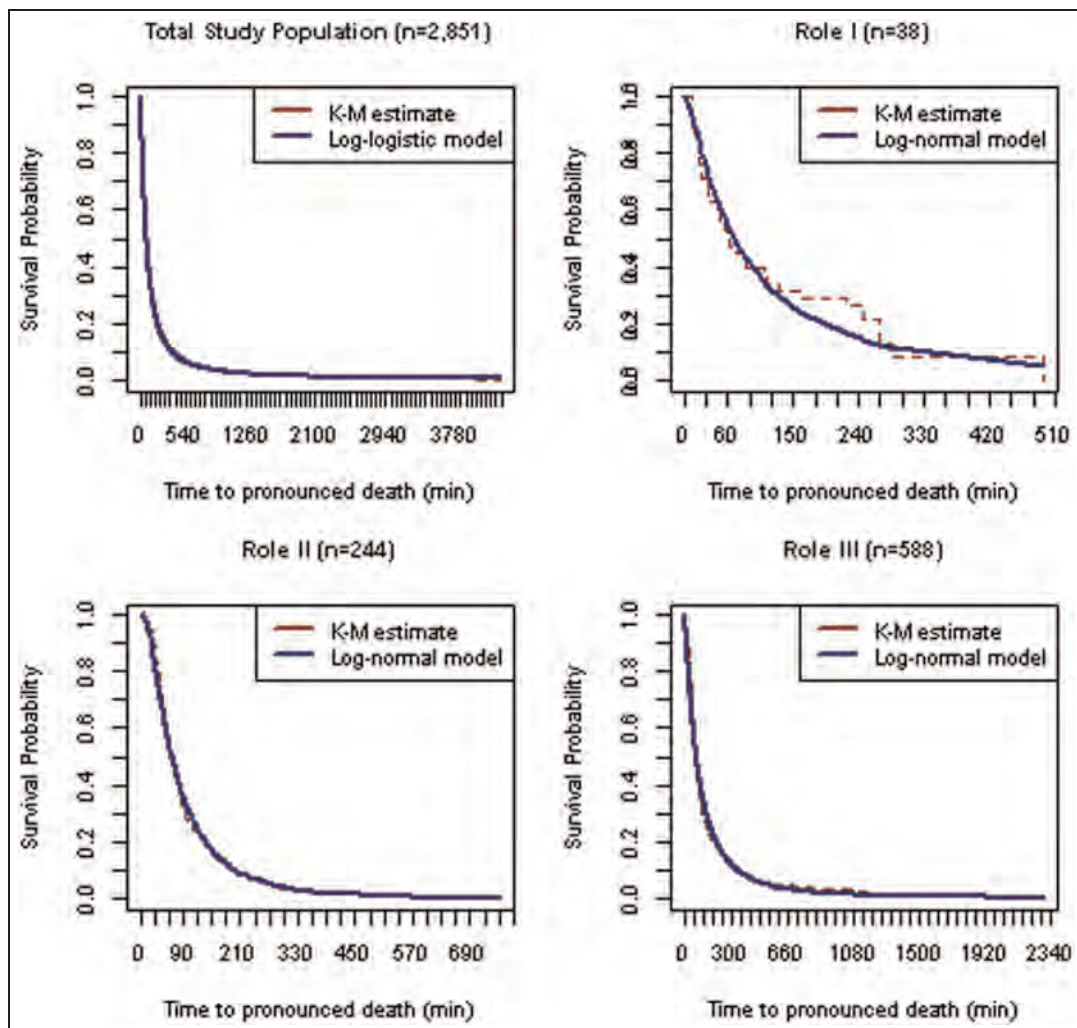


Figure 6. Empirical Kaplan–Meier survival estimates overlaid with log-normal curves for the entire study population ($n = 2851$), Role I ($n = 38$), Role II ($n = 244$) and Role III ($n = 588$).

4. Discussion

This study was undertaken to develop empirically based time-to-death curves for use in estimating times to death in medical care simulations. The evidence indicates that survival time varies across roles of care, but was at most weakly related to injury severity. These observations suggest that modeling should incorporate role of care differences and that a single model could be applied to all deaths regardless of injury severity. Survival-time modeling indicates that log-normal models provided accurate time-to-death predictions for all three roles of care. A log-logistic model would effectively simulate times to death for the overall study population, regardless of role of care.

Survival time was independent of injury severity. This initially surprising result is reasonable if a clear distinction is made between death rate and survival time. More severe injuries produce more fatalities in civilian trauma cases²¹ and combat trauma casualties.²² Indeed, this association is fundamental to injury severity scaling.¹¹ However, it takes time for trauma victims to expire, regardless of injury severity. The evidence suggests that among combat casualties the time-to-death distribution is independent of severity even though higher severity is positively correlated with an increased probability of death.

The time-to-death curve models developed above share a critical attribute in that observed survival times were estimated with high precision. Actual data times seldom fall far from the curve. This is more important than the fact that the models did not track the K-M step function with precision. The step function is constant over intervals that contain no deaths, whereas the curves treat time as the continuous function that it is. In the absence of reasons to believe that the survival-time distribution truly is a step function, the smooth, monotonically decreasing curves are a reasonable formulation of the time to death.

The modest increase in median time to death from Role I to Role III was noteworthy. Increased survival would be expected given that more extensive treatment options are available at higher roles of care. In fact, the modest size of the increases is more striking than their existence. The difference implies better quality care at higher roles given the virtually identical injury severity distributions across roles of care. The modest differences therefore might be misinterpreted as evidence that quality of care increases only slightly from Role I to Role III. This inference would not be justified because the data are limited entirely to fatalities. The proportion of survivors at each level of care increases without necessarily altering the time-to-death distributions.

The good fit of the functional models suggest that they accurately predict times over the full range of the data. This point is important in light of the gaps in the time distributions evident in the K-M plots. The good fit to the

observed data make it reasonable to believe that the empirical functions will extrapolate well to the empirically vacant time periods.

Study limitations should be kept in mind when assessing the results. The data do not indicate the casualty's history in the MTF network, that is, whether the casualty passed through some or all roles of care in the network before expiring at a given role of care. This lack of history makes it impossible to examine the efficacy of the roles of care in terms of mortality.

The role-linked cases may be biased. These included relatively few MaxAIS = 6 cases, which may be reasonable when considered in context. Some seriously injured casualties must survive only briefly and may often expire before reaching care. Assuming these cases are never linked to a specific role of care, the frequency of MaxAIS = 6 cases will be higher in the overall combat casualty population than in the treated casualty population. This explanation for the apparent bias is reasonable, but it is speculative without further evidence.

Sparse data presented some problems. Very few deaths were linked to Role I care, so the time-to-death function for the role must be viewed with caution. The low frequency may be explained by evidence that almost all seriously wounded patients are evacuated directly from the POI to Role II or Role III facilities in current operations. If so, uncertainty regarding Role I survival times can be tolerated because those times are relatively unimportant for overall medical planning. Gaps in the survival-time distributions that were evident in the K-M analysis were another instance of sparse data. The good fit of the data to the empirical time-to-death curves suggests that those curves will perform adequately when interpolated into the gaps, but the possibility that additional data would shift the curves cannot be ruled out.

The data available to compute survival time was another limitation. The requisite information was missing from many records, and the data that were available may be biased. The recorded time of death is the time the casualty was pronounced dead by a physician. This reported time will be later than the true time of death whenever the physician is not present when the casualty dies. Finally, casualties treated at higher roles of care are a mixture. Some casualties progress from lower roles to higher ones, but recent studies show that patients are being evacuated from the POI to the nearest surgical MTF. The 15% of casualty deaths at Role II and Role III care that occurred within 30 minutes from the POI suggest that many patients do not go through a hierarchical treatment process. Changes in the proportion of direct admissions might significantly alter the survival-time functions reported here.

For future work, we propose that the combat time-to-death curves be updated as more data from combat operations become available. The availability of the role of care

at which casualties died and the time of arrival at the role of care will further reduce bias in estimating the survival functions.

The temporal distribution of deaths among combat casualties can be accurately estimated from time-to-death curves. Accurate estimates of time to death are important for combat medical planners. Prior to this study, the data available to formulate those estimates was limited. The present work capitalized on recent developments in the medical data collection and communication networks for combat operations in Iraq and Afghanistan that have resulted in a much larger database for estimating survival time. The results substantially extended the state of the art, providing greater precision in parameter estimates of the curves and the resulting time-to-death estimates for individual casualties. These time-to-death curves should refine the survival-time estimates used in combat medical logistics planning.

Disclaimer

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References

- Office of the Assistant Secretary of Defense, Health Affairs, Force Health Protection and Readiness. *Joint force health protection concept of operations*. Falls Church, VA: Department of Defense; 2007, pp.23–26.
- Mitchell R, Parker J, Galarneau M, et al. Statistical modeling of combat mortality events by using subject matter expert opinions and Operation Iraqi Freedom empirical results from the Navy-Marine Corps Combat Trauma Registry. *J Defense Model Simulat* 2010; 7: 145–155.
- Mitchell R, Galarneau M, Hancock B, et al. *Modeling dynamic casualty mortality curves in the tactical medical logistics (TML+) planning tool*. Technical Report No. 04–31, 2004. San Diego, CA: Naval Health Research Center.
- Galarneau MR, Hancock WC, Konoske P, et al. The Navy-Marine Corps Combat Trauma Registry. *Mil Med* 2006; 171: 691–697.
- Gennarelli T and Wodzin E. AIS 2005: a contemporary injury scale. *Injury* 2006; 37: 1083–1091.
- Committee on Medical Aspects of Automotive Safety. Rating the severity of tissue damage. I. The abbreviated injury scale. *J Am Med Assoc* 1971; 215(2): 277–280.
- Gennarelli T and Wodzin E. *AIS© 2005 update 2008*. Des Plaines, IL: American Association for Automotive Medicine (AAAM), 2008.
- Kilgo P, Osler T and Meredith W. The worst injury predicts mortality outcome the best: rethinking the role of multiple injuries in trauma outcome scoring. *J Trauma* 2003; 55: 599–607.
- Baker S and O'Neill B. The injury severity score: an update. *J Trauma* 1976; 16: 882–885.
- Baker S, O'Neill B, Haddon W Jr, et al. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *J Trauma* 1974; 14: 187–196.
- Champion H. Trauma scoring. *Scand J Surg* 2002; 91: 12–22.
- Copes W, Champion H, Sacco W, et al. Progress in characterizing anatomic injury. *J Trauma* 1990; 30: 1200–1207.
- Meredith J, Evans G, Kilgo P, et al. A comparison of the abilities of nine scoring algorithms in predicting mortality. *J Trauma* 2002; 53: 621–629.
- Osler T, Baker S and Long W. A modification of the injury severity score that both improves accuracy and simplifies scoring. *J Trauma* 1997; 43: 922–926.
- Osler T, Rutledge R, Deis J, et al. ICISS: an international classification of disease-9 based injury severity score. *J Trauma* 1996; 41: 380–388.
- Eastridge B, Mabry R, Seguin P, et al. Death on the battlefield (2001–2011): implications for the future of combat casualty care. *J Trauma* 2012; 73: 431–437.
- Kuehl R. *Design of experiments: statistical principles of research design and analysis*. 2nd ed. Independence, KY: Duxbury Press, 2000, pp.107–111.
- Allison P. *Survival analysis using SAS: a practical guide*. 2nd ed. Cary, NC: SAS Institute, 2010, pp.29–124.
- Connock M, Hyde C and Moore D. Cautions regarding the fitting and interpretation of survival curves: examples from NICE single technology appraisals of drugs for cancer. *Pharmacoeconomics* 2011; 29: 827–837.
- Akaike H. A new look at the statistical model identification. *IEEE Trans Automat Contr* 1974; 19: 716–723.
- Tohira H, Jacobs I, Mountain D, et al. Systematic review of predictive performance of injury severity scoring tools. *Scand J Trauma Resusc Emerg Med* 2012; 20: 63.
- Eastridge B, Owsley J, Sebesta J, et al. Admission physiology criteria after injury on the battlefield predict medical resource utilization and patient mortality. *J Trauma* 2006; 61: 820–823.

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